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Soft-Tissue Myxomas and Fibrous Dysplasia of Bone

A Case Report and Review of the Literature

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An association between fibrous dysplasia and myxomas (soft-tissue neoplasms of mesenchymal origin) has been described in the literature. The authors report another such case of fibrous dysplasia/myxoma coexistence: a patient with polyostotic fibrous dysplasia who developed right anterior thigh pain from a solitary intramuscular myxoma. After a thorough review of the literature, the authors found that a causal relationship between fibrous dysplasia and myxomata remains uncertain. To ensure an adequate and accurate diagnosis, however, patients with soft-tissue myxomas should be thoroughly evaluated for fibrous dysplasia. A proper investigation of soft-tissue masses also should be carried out to exclude malignancy.

Fibrous dysplasia involves a localized area of bone in which the normal architecture has been deformed by a dysplastic proliferation of fibrous connective tissue containing immature woven bone. The cause of this benign process is unknown. Single bone (monostotic) and multiple bone (polyostotic) forms have been identified. Systemic manifestations also may be present.[4,8,28] Fibrous dysplasia and some of its systemic manifestations were recognized earlier in this century.[1,11,24,25,31] In 1922, Weil[31] first described the association of skeletal fibrous dysplasia with endocrine abnormalities (especially precocious puberty) and cutaneous hyperpigmentation, a condition known today as the McCune-Albright syndrome. Lichtenstein and Jaffe[18,19] were first to use the definitive term, "fibrous dysplasia".

Soft-tissue myxomas are benign neoplasms of mesenchymal origin in which relatively few, stellate-shaped cells are seen in an abundant, mucopolysaccharide-rich matrix. Frequently, these neoplasms are traversed by a loose network of thin collagen bundles. Their gross appearance and clinical behavior are sometimes mistaken for sarcomas, especially myxoid liposarcomas. Despite a reasonable prevalence of myxomas, they are seldom reported in the literature.[9,14] Variable in size and seen almost exclusively in adults, their principal location is within skeletal muscle; however, they have appeared in retroperitoneal tissue, bone (especially jaw), and subcutaneous tissue. The origin of these tumors remains unclear.[9,10,23,29,33]

The first reported association of soft-tissue myxomas and fibrous dysplasia was in 1926 by Henschen.[13] Since then, 19 other cases have been recorded in American and European literature. There are four reported cases of McCune-Albright syndrome.[4–6,12,14–17,20–23,27,30,33,34]

CASE REPORT

A 36-year-old woman was examined in August 1985. She complained of constant and progressive right anterior thigh pain. She had a history of polyostotic fibrous dysplasia and multiple fractures since age five with known involvement in the right femur, right innominate bone, and right first and

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tenth ribs. The patient had been in a minor motor vehicle accident five weeks before presentation without known trauma to the right lower extremity. One week after the accident, she developed pain in her right thigh, which subsided within a few days and then returned four weeks later. She also noticed a tender mass in that same area. The pain was progressive and interfered with ambulation. There was no fever, generalized weakness, fatigue, weight loss, or endocrine abnormality (including precocious puberty).

Physical examination disclosed a 6 × 6-cm, firm, movable, tender, nonpulsating mass of the right anterior proximal thigh. There were no skin changes or increased warmth over the area of the mass. The patient had a slight antalgic gait toward the right and the range of motion of her right hip was limited in abduction to 20°. There was mild to moderate pain in the hip joint to extremes of motion. Full range of motion at her right knee and ankle were recorded. Some posterior bowing of the right femur was noted. Neurovascular examination of the right leg was within normal limits, and there was no lymphadenopathy or muscle atrophy. No thyromegaly was noted. Skin examination showed multiple, large, brown maculae over the back. There was a small cyst of the interphalangeal joint of her right thumb.

Plain films of her right femur demonstrated multiple radiolucent lesions along with posterior bowing and irregular widening of the shaft, changes consistent with fibrous dysplasia (Fig. 1). An undisplaced fracture of the right superior pubic ramus also was noted. Roentgenograms and tomograms of the pelvis demonstrated long-standing changes of fibrous dysplasia and confirmed the right superior pubic ramus fracture. No fracture was visualized in the femur corresponding to the area of the painful mass. A ^{99m}Tc bone scan showed increased uptake of the entire right femur, right innominate bone, right first rib, and right superior pubic ramus. The chest roentgenogram was normal. Lumbosacral spine films showed mild degenerative changes. Computed tomography scan of the right thigh with intravenous contrast demonstrated a mass of soft-tissue density starting just below the inguinal ligament and extending inferiorly to a size of approximately 8 × 6 × 6 cm (Fig. 2). No bony or neurovascular involvement was appreciated. A right femoral arteriogram demonstrated the mass to be relatively avascular. Nerve conduction studies of the right lower extremity yielded normal results.

The patient was taken to the operating room for an incisional biopsy of the right anterior thigh mass under general anesthesia. Permanent section studies revealed an intramuscular myxoma of the right rectus femoris muscle. The patient had a wide excision of the myxoma. She did well after operation and has had no recurrence to date.

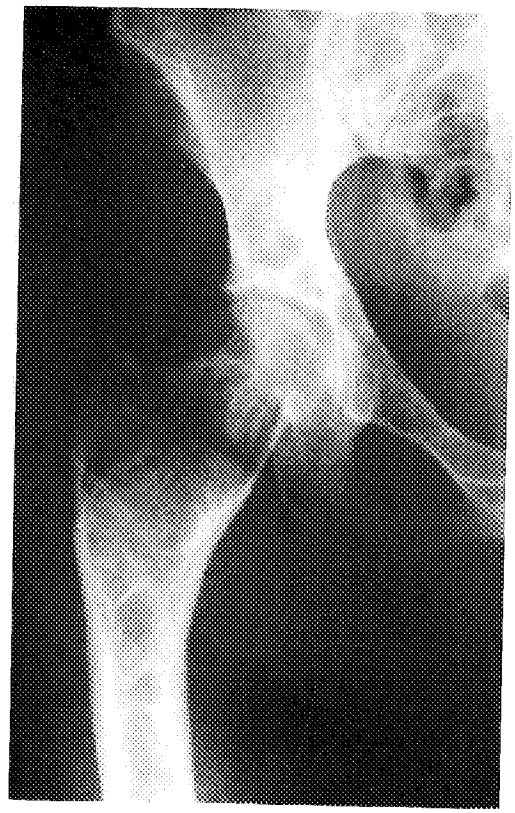

FIG. 1. Plain anteroposterior roentgenograph of right proximal femur and hip. Multiple radiolucent areas are seen throughout the femur and in portions of the right innominate bone. These are consistent with the patient's known history of fibrous dysplasia with involvement in these areas. The classic roentgenographic "ground glass" appearance of fibrous dysplasia is evident in certain regions. Although not visible here, posterior bowing of the right femur was demonstrated on other roentgenograms.

Grossly, the lesion was a firm, encapsulated, rounded neoplasm weighing 75 g and measuring 9 × 4.5 × 4.5 cm. The capsule was intact and bosselated gray. Cut surfaces showed a gray, translucent myxoid neoplasm subdivided by delicate white trabeculae into 0.3–2.0-cm nodules (Fig. 3). No fibrotic areas or cysts were evident. Microscopic sections showed a myxoid neoplasm of fairly uniform, stellate cells within a mucinous matrix with intermittent collagen bundles. Blood vessels were

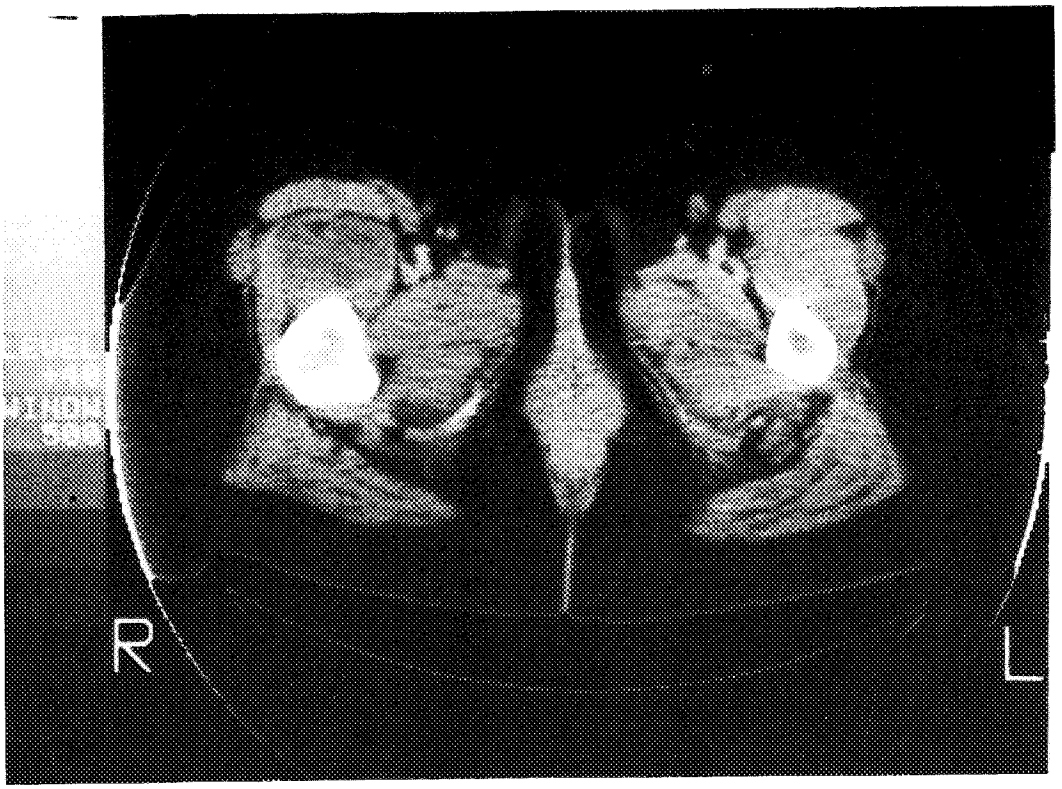

FIG. 2. Computed tomography at thigh level. A rather large mass of soft-tissue density is demonstrated on this view in the right rectus femoris muscle region. Also of note is the large diameter of the femur itself on the right.

inconspicuous except at the periphery, which was slightly more cellular. No lipoblasts, rhabdomyoblasts, pleomorphism, or mitotic figures were identified.

DISCUSSION

The patient was diagnosed with fibrous dysplasia at age five and with an intramuscular myxoma at age 36. A review of the literature showed 21 cases of fibrous dysplasia with an age range of infancy to 57 years. Sixty-two percent were diagnosed before the third decade of life. Initial presentation for a myxoma ranged from 17 to 82 years, with 71% ranging from 30 to 70 years. This is an age range curve similar to that of myxomas without fibrous dysplasia. In all but one case, the myxomas were noted anywhere from years to decades after the diagnoses of fibrous dysplasia (Table 1).

Although fibrous dysplasia is most commonly seen in its monostotic form, the polyostotic form was most often associated with myxomas. Likewise, the myxomas, which usually are solitary, tended toward multiplicity when present with fibrous dysplasia. Symptoms were typical for fibrous dysplasia, with pathologic fractures being the most common presentation. Blaiser *et al.*[5] reported a case in which the patient was unaware of her fibrous dysplasia until a diagnosis was made from roentgenograms taken to evaluate a myxoma.

Systemic manifestations of fibrous dysplasia are well recognized.[2–4,8,26,28,34] These manifestations present as endocrine and cutane-

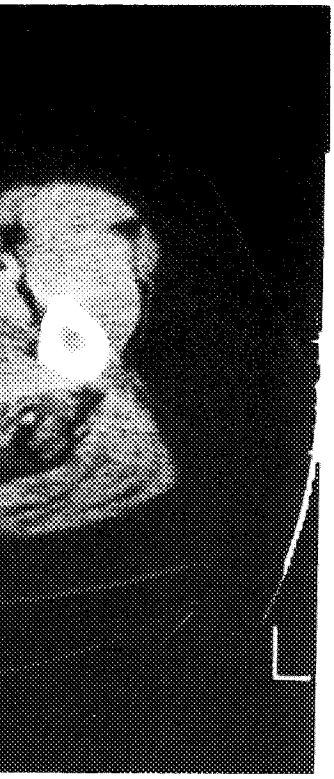

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FIG. 3. Cut specimen of solitary myxoma. The gelatinous neoplasm is subdivided into nodules by fibrotic tissue.

ous disorders, with precocious puberty and skin hyperpigmentation being most common. Other skeletal lesions (both benign and malignant) occurring in areas with fibrous dysplasia have been reported, ranging from aneurysmal bone cysts and desmoplastic fibromas to various bone sarcomas.[7,23,32,33,34] Two malignant bone lesions were recorded in patients with fibrous dysplasia and myxomas.[22,34] Both were osteogenic sarcomas, the most common malignant skeletal neoplasms associated with fibrous dysplasia. Both were located in areas of fibrous dysplastic lesions and were believed to be transformations from the benign bone disease. Neither patient had previously received irradiation. The reported incidence of malignant transformation in fibrous dysplasia has been 0.4–0.5%.[34] Currently, the implication of malignant transformation in fibrous dysplasia remains unknown. Its presence, however, should direct attention to careful workup, management, and follow-up care for any patient with fibrous dysplasia, myxomas, or malignant bone lesions.

Prognosis and treatment for fibrous dysplasia when associated with myxomas is similar to that of fibrous dysplasia alone. The presence of a myxoma appears to have no influence on the severity or progression of the fibrous dysplasia. An interesting possibility exists, that is, that the prevalence of this association may actually be greater than reflected in the literature because of the significant asymptomatic nature of each component.

Several researchers have noted that myxomas appear in close proximity to the region of the most severely affected bone.[6,30,33] A contiguous connection between the myxoma and a fibrous dysplastic lesion has never been

TABLE 1. Cases of Soft-Tissue Myxomas With Fibrous Dysplasia of Bone

Author	Gender	Age at Diagnosis		Location			Comments
		Fibrous Dysplasia (yrs)	*Myxoma (yrs)*	*Fibrous Dysplasia*	*Myxoma*	*Cafe-au-lait Spots*	
Henschen 1926	F	Child	66*	R thigh	R thigh		
Krogius 1929	F	6	26	Bilateral	R thigh		
Uehlinger 1940	M	11	67	Bilateral	R thigh		
Braunwarth 1953	F	NR	55	Left (M)	Left		
Mazabraud and Girard 1957	M	22	54	Right	Right (S)		
Heinemann and Woerth 1958	M	18	82	Right	Right	Right	Goiter
LaPorte *et al.* 1961	F	12	24	Right	Right	Right	Precocious puberty, hyperthyroid
Lick and Viehweger 1962	M	18	59	Bilateral	Right		Goiter
Mazabraud *et al.* 1967	F	Infant	NR	Right	Right	Right	Precocious puberty, osteosarcoma
Wirth *et al.* 1971	M	3	17	Bilateral	L arm/chest	L shoulder	Cafe-au-lait spots only
Wirth *et al.* 1971	M	20	33	Bilateral	R arm/thigh	R skull	Cafe-au-lait spots only, pagetoid skull changes
Ireland *et al.* 1973	F	NR	49	L femur (M)	Bilateral		Lipomas
	F	NR	61	R hip/femur	R thigh		"Abdominal tumors"
	F	23	28	L leg	L leg		Fibrosarcoma of breast
Logel 1976	F	Child	41	Bilateral	R leg	R trunk	Precocious puberty, diabetes mellitus, hyperthyroid, pagetoid skull changes
Sedmack *et al.* 1983	M	33	50s	L leg	L thigh		Lipoma, "soft spot" of left femur
Lever and Pettingale 1983	F	1	50	Bilateral	R thigh (S)		Precocious puberty, hypophosphatemic osteomalacia
Witkin *et al.* 1986	M	15	40	Bilateral	L thigh (S)		Osteogenic sarcoma, hemoglobin J Baltimore and S
Blaiser *et al.* 1986	F	57	55	Left	Chest/L thigh		
Biagini *et al.* 1987	F	10	42	Bilateral	Left		
Prayson and Leeson 1990	F	5	36	Bilateral	R thigh (S)	Back	Cafe-au-lait spots only, ganglion/ carpel tunnel syndrome R hand

NR, not reported; (M), monostotic; (S), solitary; * age at autopsy.

							Lipoma, "soft spot" of left femur
Sedmack *et al.* 1983	M	33	50s	L leg	L thigh		Precocious puberty, hypophosphatemic osteomalacia
Lever and Pettingale 1983	F	1	50	Bilateral	R thigh (S)		
Witkin *et al.* 1986	M	15	40	Bilateral	L thigh (S)		Osteogenic sarcoma, hemoglobin J Baltimore and S
Blaiser *et al.* 1986	F	57	55	Left	Chest/L thigh		
Biagini *et al.* 1987	F	10	42	Bilateral	Left		
Prayson and Leeson 1990	F	5	36	Bilateral	R thigh (S)	Back	Cafe-au-lait spots only, ganglion/ carpel tunnel syndrome R hand

NR, not reported; (M), monostotic; (S), solitary; * age at autopsy.

established, however. In addition, the number and size of myxomas and dysplastic lesions occur irrespective of each other. Although myxomas are frequently found to occur singly, 81% of the patients had multiple myxomas occurring with fibrous dysplasia. The patient in the case report was one of only four with a solitary myxoma. The most prevalent location for myxomas was the thigh.

Because myxomas are benign and do not metastasize, simple local excision is usually sufficient. With underlying bony lesions present and a significant number of patients who present with pain, however, it seems essential for the clinician to consider more aggressive entities—such as sarcomas. In addition, reports of malignant transformation of fibrous dysplasia reemphasize the importance of a proper evaluation for malignant neoplasm. There has been no report describing malignant degeneration of a myxoma and no evidence supporting trauma as a predisposing factor to initial myxoma appearance.

After adequate excision, recurrence of myxomas in the setting of fibrous dysplasia is rare. Only one case has been reported.[21] Regardless of an association with fibrous dysplasia, when a myxoma recurs after ample excision, the possibility of a more aggressive entity, such as myxoid liposarcoma must be considered. The overall prognosis for myxomas is excellent, however.

The causal relationship between fibrous dysplasia and soft-tissue myxomas remains unclear. Henschen[13] recognized the association but was uncertain of the cause. Krogius[15] emphasized a shared disturbance of development and mentioned a genetic relationship between the lesions. Uehlinger[30] supported a similar but uncertain origin. Braunwarth[6] discussed a strong similarity between fibrous dysplasia with myxomas and neurofibromatosis, whereas Mazabraud and Girard[22] reiterated the concept of a common histogenesis, suggesting an abnormal development of bone and tendon. In an effort to explain the large time discrepancy between the two lesions, Wirth *et al.*[33] proposed that a basic error in tissue metabolism persisted years beyond initial growth and was restricted to the region or regions of bony involvement. Ireland *et al.*[14] reported an error of tissue metabolism to be an attractive hypothesis.

A common error in tissue metabolism does, in fact, appear attractive for a regional disturbance. Yet, many questions remain unanswered. Why do relatively few patients with fibrous dysplasia develop myxomas and vice versa? How does the small but significant malignant transformation of fibrous dysplasia relate to the overall picture? Can the associated endocrine abnormalities also be attributed to an inborn error of metabolism? Only by finding answers to questions such as these can we approach a full understanding of this unusual association.

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